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NOTICE OF ALLOWANCE AND FEE(S) DUE

26646 7590 12/02/2003

KENYON & KENYON
ONE BROADWAY
NEW YORK, NY 10004

EXAMINER	
NGUYEN, DAVE TRONG	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/02/2003

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/750,779	01/02/2001	Wei-ping Li	12013/55202	7468

TITLE OF INVENTION: CONTROLLED DELIVERY OF THERAPEUTIC AGENTS BY INSERTABLE MEDICAL DEVICES

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1330	$300	$1630	03/02/2004

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:
A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status is changed, pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above and notify the United States Patent and Trademark Office of the change in status, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above.

☐ Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 4 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Legibly mark-up with any corrections or use Block 1)

26646 7590 12/02/2003

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Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO, on the date indicated below.

(Depositor's name)

(Signature)

(Date)

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nonprovisional	NO	$1330	$300	$1630	03/02/2004

EXAMINER	ART UNIT	CLASS-SUBCLASS
NGUYEN, DAVE TRONG	1632	514-044000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the USPTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent); ❑ individual ❑ corporation or other private group entity ❑ government

4a. The following fee(s) are enclosed:

❑ Issue Fee

❑ Publication Fee

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s):

❑ A check in the amount of the fee(s) is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The Director is hereby authorized by charge the required fee(s), or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

Director for Patents is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above.

(Authorized Signature) (Date)

NOTE; The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

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Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (703) 305-1383. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

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Notice of Fee Increase on October 1, 2003

If a reply to a "Notice of Allowance and Fee(s) Due" is filed in the Office on or after October 1, 2003, then the amount due will be higher than that set forth in the "Notice of Allowance and Fee(s) Due" since there will be an increase in fees effective on October 1, 2003. See Revision of Patent Fees for Fiscal Year 2004; Final Rule, 68 Fed. Reg. 41532, 41533, 41534 (July 14, 2003).

The current fee schedule is accessible from (http://www.uspto.gov/main/howtofees.htm).

If the fee paid is the amount shown on the "Notice of Allowance and Fee(s) Due" but not the correct amount in view of the fee increase, a "Notice of Pay Balance of Issue Fee" will be mailed to applicant. In order to avoid processing delays associated with mailing of a "Notice of Pay Balance of Issue Fee," if the response to the Notice of Allowance is to be filed on or after October 1, 2003 (or mailed with a certificate of mailing on or after October 1, 2003), the issue fee paid should be the fee that is required at the time the fee is paid. If the issue fee was previously paid, and the response to the "Notice of Allowance and Fee(s) Due" includes a request to apply a previously-paid issue fee to the issue fee now due, then the difference between the issue fee amount at the time the response is filed and the previously-paid issue fee should be paid. See Manual of Patent Examining Procedure, Section 1308.01 (Eighth Edition, August 2001).

Effective October 1, 2003, 37 CFR 1.18 is amended by revising paragraphs (a) through (c) to read as set forth below.

Section 1.18 Patent post allowance (including issue) fees.

(a) Issue fee for issuing each original or reissue patent, except a design or plant patent:
By a small entity (Sec. 1.27(a)) $665.00
By other than a small entity $1,330.00

(b) Issue fee for issuing a design patent:
By a small entity (Sec. 1.27(a)) $240.00
By other than a small entity $480.00

(c) Issue fee for issuing a plant patent:
By a small entity (Sec. 1.27(a)) $320.00
By other than a small entity $640.00

Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

Notice of Allowability	Application No.	Applicant(s)	
	09/750,779	LI ET AL.	
	Examiner	Art Unit	
	Dave T Nguyen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *September 22, 2003*.
2. ☒ The allowed claim(s) is/are *1-5, 7-8, 10-14, 16-17, 19-23, 25-26, 28-32, 34-35, 37-42, 44--66*.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.
5. ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
   (a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
8. ☒ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☒ to Paper No. *11*.
   (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
   (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the margin according to 37 CFR 1.121(d).

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1☐ Notice of References Cited (PTO-892)
2☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No. _____
4☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5☐ Notice of Informal Patent Application (PTO-152)
6☐ Interview Summary (PTO-413), Paper No._____ .
7☒ Examiner's Amendment/Comment
8☐ Examiner's Statement of Reasons for Allowance
9☐ Other

Claims 6, 9, 15, 18, 24, 27, 33, 36, and 43 have been canceled, claims 1, 3, 4, 7, 8, 10, 16, 17, 19, 20, 25, 26, 28, 29, 34, 35, 38, 39, 44, 45, 47, 49, 50, 52-56, 58, 59, and 61-66 have been amended, and claims 67-70 have been added by the amendment filed August 27, 2003. The specification has been amended by the amendment after final dated September 22, 2003.

Examiner' s Amendment

An examiner's amendment to the record appears below. An extension of time under 37 CFR 1.136(a) is required in order to make an examiner's amendment which places this application in condition for allowance. During a telephone conversation conducted on November 19, 2003, Attorney Zeba Ali requested an extension of time for 3 MONTH(S) and authorized the Commissioner to charge Deposit Account No.11-0600 the required fee of $ 950 for this extension and authorized the following examiner's amendment. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Attorney Zeba Ali on November 19, 2003.

AMENDMENTS TO THE CLAIMS:

1. (Currently Amended) An implantable medical device comprising a coating on at least a portion thereof, said coating comprising:

an inner layer of a cationic polyelectrolyte carrier; ~~and~~

a layer of at least one negatively charged therapeutic agent adsorbed onto said inner layer of a cationic polyelectrolyte carrier; and

an additional layer or layers of a cationic polyelectrolyte carrier and an additional layer or layers of at least one negatively charged therapeutic agent adsorbed onto said additional layer or layers of a cationic polyelectrolyte carrier, wherein said additional layer or layers of a ~~polyelectrolye~~ polyelectrolyte carrier and said additional layer or layers of at least one negatively charged therapeutic agent alternate.

2. (Currently Amended) The medical device of claim 1, further comprising an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner or additional layer or layers of a cationic polyelectrolyte carrier.

3. (Currently Amended) The medical device of claim 2, wherein the outermost layer of a cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than ~~at least one of~~ the inner or additional layer or layers of a cationic polyelectrolyte carrier.

4. (Currently Amended) The medical device of claim 1, wherein ~~at least one of~~ the inner or additional layer or layers of a cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

5. (Original) The medical device of claim 1, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

6. (Cancelled).

7. (Previously Presented) The medical device of claim 1, wherein the at least one negatively charged therapeutic agent comprises rapamycin.

7

8. (Previously Presented) The medical device of claim 1, wherein the at least one negatively charged therapeutic agent comprises paclitaxel.

9. (Cancelled)

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10. (Currently Amended) A method of adsorbing at least one negatively charged therapeutic agent onto a medical device comprising:

(a) coating at least a portion of a medical device with a cationic polyelectrolyte carrier to form an inner layer of a cationic polyelectrolyte carrier;

(b) washing the inner layer of a cationic polyelectrolyte carrier with a washing solution;

(c) adsorbing at least one negatively charged therapeutic agent onto the inner layer of a cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and ~~optionally~~

(d) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of a cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

9 8

11. (Currently Amended) The method of claim 10, further comprising the step of coating the outermost layer of the at least one negatively charged therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of a cationic polyelectrolyte carrier.

10 9

12. (Currently Amended) The method of claim 11, wherein the outermost layer of a cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than ~~at least one of~~ the inner layer or multiple layers of a cationic polyelectrolyte carrier.

B

13. (Currently Amended) The method of claim 10, wherein ~~at least one of~~ the inner layer or multiple layers of a cationic polyelectrolyte carrier comprises a human serum albumin, gelatin, chitosan, or a combination thereof.

14. (Original) The method of claim 10, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

15. (Cancelled).

16. (Previously Presented) The method of claim 10, wherein the at least one negatively charged therapeutic agent comprises rapamycin.

17. (Previously Presented) The method of claim 10, wherein the at least one negatively charged therapeutic agent comprises paclitaxel.

18. (Cancelled)

19. (Currently Amended) A medical device comprising at least one negatively charged therapeutic agent adsorbed on at least a portion thereof and produced by a process comprising:

(a) coating at least a portion of a medical device with a cationic polyelectrolyte carrier to form an inner layer of a cationic polyelectrolyte carrier;

(b) washing the inner layer of a cationic polyelectrolyte carrier with a washing solution;

(c) adsorbing at least one negatively charged therapeutic agent onto the inner layer of a cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and ~~optionally~~

(d) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of a cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until

a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

20. (Currently Amended) The medical device of claim 19, wherein the process further comprises the step of coating the outermost layer of the at least one negatively charged therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of a cationic polyelectrolyte carrier.

21. (Currently Amended) The method of claim 20, wherein the outermost layer of a cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than ~~at least one of~~ the inner layer or multiple layers of a cationic polyelectrolyte carrier.

22. (Currently Amended) The medical device of claim 19, wherein ~~at least one of~~ the inner layer or multiple layers of a cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

23. (Original) The medical device of claim 19, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

24. (Cancelled)

25. (Previously Presented) The medical device of claim 19, wherein the at least one negatively charged therapeutic agent comprises rapamycin.

26. (Previously Presented) The medical device of claim 19, wherein the at least one negatively charged therapeutic agent comprises paclitaxel.

27. (Cancelled)

~~28~~ 22. (Currently Amended) A method of delivering a therapeutic agent to a target location by implanting in the target location a medical device comprising at least one negatively charged therapeutic agent adsorbed on at least a portion thereof; wherein the medical device is produced by a process comprising:

(a) coating at least a portion of a medical device with a cationic polyelectrolyte carrier to form a layer of a cationic polyelectrolyte carrier;

(b) washing the layer of a cationic polyelectrolyte carrier with a washing solution;

(c) adsorbing at least one negatively charged therapeutic agent onto the layer of a cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and ~~optionally~~

(d) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of a cationic polyelectrolyte carrier and therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

~~29~~ 23. (Currently Amended) The method of claim ~~28~~ 22, further comprising the step of coating the outermost layer of the at least one negatively charged therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of a cationic polyelectrolyte carrier.

~~30~~ 24. (Currently Amended) The method of claim ~~29~~ 23, wherein the outermost layer of a cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than ~~at least one of~~ the inner layer or multiple layers of a cationic polyelectrolyte carrier.

~~31~~ 25. (Original) The method of claim ~~28~~ 22, wherein ~~at least one of~~ the inner layer or multiple layers of a cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

~~32~~ 26. (Original) The method of claim ~~28~~ 22, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

33. (Cancelled)

34. (Previously Presented) The method of claim 28, wherein the at least one negatively charged therapeutic agent comprises rapamycin.

35. (Previously Presented) The method of claim 28, wherein the at least one negatively charged therapeutic agent comprises paclitaxel.

36. (Cancelled)

37. (Previously Presented) The method of claim 28, wherein the target location comprises at least one location selected from the group consisting of brain, heart, liver, skeletal muscle, smooth muscle, kidney, bladder, intestines, stomach, pancreas, ovary, prostate, cartilage, bone, lung, blood vessel, ureter, urethra, and testes.

38. (Currently Amended) A method for treating the occurrence or severity of a clinical disease or condition, comprising:

(a) preparing a medical device by:

(i) coating at least one a portion of a medical device with a cationic polyelectrolyte carrier to form a layer of a cationic polyelectrolyte carrier;

(ii) washing the layer of a cationic polyelectrolyte carrier with a washing solution;

(iii) adsorbing at least one negatively charged therapeutic agent effective to treat or reduce the occurrence of the clinical disease or condition onto the layer of a cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and ~~optionally~~

(iv) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of a cationic polyelectrolyte carrier and at least one negatively

charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.; and

(b) implanting the medical device into a target location in a mammal from which the at least one negatively charged therapeutic agent can treat or reduce the occurrence or severity of the clinical disease or condition.

31 30
~~39~~. (Currently Amended) The method of claim ~~38~~, further comprising the step of coating the outermost layer of at least one negatively charged therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of a cationic polyelectrolyte carrier.

32 31
~~40~~. (Currently Amended) The method of claim ~~39~~, wherein the outermost layer of a cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than ~~at least one of~~ the inner layer or multiple layers of a cationic polyelectrolyte carrier.

33 30
~~41~~. (Currently Amended) The method of claim ~~38~~, wherein ~~at least one of~~ the inner layer or multiple layers of a cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

34 30
~~42~~. (Original) The method of claim ~~38~~, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

43. (Cancelled)

35 30
~~44~~. (Currently Amended) The method of claim ~~38~~, wherein the clinical disease or condition comprises restenosis or angiogenesis and [theat] the at least one negatively charged therapeutic agent comprises rapamycin.

36 30
~~45~~. (Previously Presented) The method of claim ~~38~~, wherein the clinical disease or condition comprises a malignancy or malignant cell growth and the at least one negatively charged therapeutic agent comprises paclitaxel.

37 30
~~46~~. (Previously Presented) The method of claim ~~38~~, wherein the target location comprises at least one location selected from the group consisting of brain, heart, liver, skeletal muscle, smooth muscle, kidney, bladder, intestines, stomach, pancreas, ovary, prostate, cartilage, bone, lung, blood vessel, ureter, urethra, and testes.

38
~~47~~. (Currently Amended) The medical device of claim 1 wherein the at least one negatively charged therapeutic agent is selected from the group consisting of a: anti-thrombogenic protein, antioxidant compound, angiogenic protein, agent which blocks smooth muscle cell proliferation, anti-inflammatory agent, calcium entry blocker, antineoplastic/antiproliferative/anti-mitotic compound, anti-microbial compound, anesthetic agent, nitric oxide donor, anti-coagulant, vascular cell growth promoting protein, vascular cell growth protein inhibitor, vascular cell growth antibody inhibitor, cholesterol lowering drug, vasodilating drug, protein that protects against cell death, cell cycle CDK protein inhibitor, anti-restenosis protein, agent for treating malignancies, bone morphogenic protein, ~~and~~ a polynucleotide encoding any of the above named proteins or protein inhibitors, and an adenovirus vector comprising a polynucleotide encoding any of the above named proteins or protein inhibitors.

39 38
~~48~~. (Previously Presented) The medical device of claim ~~47~~ wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

40 38
~~49~~. (Previously Presented) The medical device of claim ~~47~~ wherein the antioxidant compound is probucol or retinoic acid.

41 9
~~50~~. (Currently Amended) The method of claim ~~10~~ wherein [theat] the at least one negatively charged therapeutic agent is selected from the group consisting of a: anti-thrombogenic protein, antioxidant compound, angiogenic protein, agent which blocks smooth muscle cell proliferation,

anti-inflammatory agent, calcium entry blocker, antineoplastic/antiproliferative/anti-mitotic compound, anti-microbial compound, anesthetic agent, nitric oxide donor, anti-coagulant, vascular cell growth promoting protein, vascular cell growth protein inhibitor, vascular cell growth antibody inhibitor, cholesterol lowering drug, vasodilating drug, protein that protects against cell death, cell cycle CDK protein inhibitor, anti-restenosis protein, agent for treating malignancies, bone morphogenic protein, ~~and~~ a polynucleotide encoding any of the above named proteins or protein inhibitors, and an adenovirus vector comprising a polynucleotide encoding any of the above named proteins or protein inhibitors.

42 41
~~51~~. (Previously Presented) The method of claim ~~50~~ wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

43 41
~~52~~. (Previously Presented) The method of claim ~~50~~ wherein the antioxidant compound is probucol or retinoic acid.

44 15
~~53~~. (Currently Amended) The medical device of claim ~~19~~ wherein the at least one negatively charged therapeutic agent is selected from the group consisting of a: anti-thrombogenic protein, antioxidant compound, angiogenic protein, agent which blocks smooth muscle cell proliferation, anti-inflammatory agent, calcium entry blocker, antineoplastic/antiproliferative/anti-mitotic compound, anti-microbial compound, anesthetic agent, nitric oxide donor, anti-coagulant, vascular cell growth promoting protein, vascular cell growth protein inhibitor, vascular cell growth antibody inhibitor, cholesterol lowering drug, vasodilating drug, protein that protects against cell death, cell cycle CDK protein inhibitor, anti-restenosis protein, agents for treating malignancies, bone morphogenic protein, ~~and~~ a polynucleotide encoding any of the above named proteins or protein inhibitors, and an adenovirus vector comprising a polynucleotide encoding any of the above named proteins or protein inhibitors.

45 44
~~54~~. (Previously Presented) The medical device of claim ~~53~~ wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

55. (Previously Presented) The medical device of claim 53 wherein the antioxidant compound is probucol or retinoic acid.

56. (Currently Amended) The method of claim 28 wherein the at least one negatively charged therapeutic agent is selected from the group consisting of a: anti-thrombogenic protein, antioxidant compound, angiogenic protein, agent which blocks smooth muscle cell proliferation, anti-inflammatory agent, calcium entry blocker, antineoplastic/antiproliferative/anti-mitotic compound, anti-microbial compound, anesthetic agent, nitric oxide donor, anti-coagulant, vascular cell growth promoting protein, vascular cell growth protein inhibitor, vascular cell growth antibody inhibitor, cholesterol lowering drug, vasodilating drug, protein that protects against cell death, cell cycle CDK protein inhibitor, anti-restenosis protein, agent for treating malignancies, bone morphogenic protein, ~~and~~ a polynucleotide encoding any of the above named proteins or protein inhibitors, and an adenovirus vector comprising a polynucleotide encoding any of the above named proteins or protein inhibitors.

57. (Previously Presented) The method of claim 56 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

58. (Previously Presented) The method of claim 56 wherein the antioxidant compound is probucol or retinoic acid.

59. (Currently Amended) The method of claim 38 wherein the at least one negatively charged therapeutic agent is selected from the group consisting of a: anti-thrombogenic protein, antioxidant compound, angiogenic protein, agent which blocks smooth muscle cell proliferation, anti-inflammatory agent, calcium entry blocker, antineoplastic/antiproliferative/anti-mitotic compound, anti-microbial compound, anesthetic agent, nitric oxide donor, anti-coagulant, vascular cell growth promoting protein, vascular cell growth protein inhibitor, vascular cell growth antibody inhibitor, cholesterol lowering drug, vasodilating drug, protein that protects against cell death, cell cycle CDK protein inhibitor, anti-restenosis protein, agentfor treating

malignancies, bone morphogenic protein, ~~and~~ a polynucleotide encoding any of the above named proteins or protein inhibitors, and an adenovirus vector comprising a polynucleotide encoding any of the above named proteins or protein inhibitors.

60. (Previously Presented) The method of claim ~~59~~ 50 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

61. (Previously Presented) The method of claim ~~59~~ 50 wherein the antioxidant compound is probucol or retinoic acid.

62. (Currently Amended) A method of delivering a therapeutic agent to a mammal, the method comprising implanting a medical device at a desired location or tissue in a mammal, wherein the medical device is produced by a process comprising:

(a) coating at least a portion of the medical device with a cationic polyelectrolyte carrier to form a layer of a cationic polyelectrolyte carrier;

(b) washing the layer of a cationic polyelectrolyte carrier with a washing solution;

(c) adsorbing at least one negatively charged therapeutic agent onto the layer of a cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and ~~optionally~~

(d) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of a cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

63. (Currently Amended) A method of delivering a polynucleotide encoding a protein to a mammal, the method comprising implanting a medical device at a desired location or tissue in a mammal, wherein the medical device is prepared by:

(i) coating at least a portion of the medical device with a cationic polyelectrolyte carrier to form a layer of a cationic polyelectrolyte carrier;

(ii) washing the layer of a cationic polyelectrolyte carrier with a washing solution;
(iii) adsorbing at least one negatively charged therapeutic agent onto the layer of a cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and ~~optionally~~
(iv) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of a cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of the at least one negatively charged therapeutic agent has been adsorbed onto the medical device~~;~~, wherein the at least one negatively charged therapeutic agent is a ~~the~~ polynucleotide encoding a protein.

55. (Currently Amended) A method of delivering a DNA encoding a therapeutic protein to a mammal, the method comprising implanting a medical device at a desired location or tissue in a mammal, wherein the medical device is prepared by:
(i) coating at least a portion of the medical device with a cationic polyelectrolyte carrier to form a layer of a cationic polyelectrolyte carrier;
(ii) washing the layer of a cationic polyelectrolyte carrier with a washing solution;
(iii) adsorbing at least one negatively charged therapeutic agent onto the layer of a cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and ~~optionally~~
(iv) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device~~;~~, wherein the at least one negatively charged therapeutic agents is a DNA encoding a therapeutic protein, wherein the therapeutic protein is selected from the group consisting of a anti-thrombogenic protein, angiogenic protein, vascular cell growth promoting protein, vascular cell growth protein inhibitor, protein that protectsagainst cell death, cell cycle CDK protein inhibitor, anti-restenosis protein, and a bone morphogenic protein.

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65. (Currently Amended) A method for inhibiting restenosis or the growth of tumor cells in a mammal, comprising:

(a) preparing a medical device by:

(i) coating at least a portion of the medical device with a cationic polyelectrolyte carrier to form a layer of a cationic polyelectrolyte carrier;

(ii) washing the layer of a cationic polyelectrolyte carrier with a washing solution;

(iii) adsorbing at least one negatively charged therapeutic agent effective to inhibit restenosis or the growth of tumor cells onto the layer of a cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and ~~optionally~~

(iv) washing the layer of negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of a cationic polyelectrolyte carrier and at least one negatively [chargd]charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device; and

(b) implanting the medical device into a target location in a mammal,[;]

wherein the at least one negatively charged therapeutic agent is a DNA coding for an anti-proliferative protein.

57

66. (Currently Amended) A method for inducing the growth of blood vessels at a target location in a mammal, comprising:

(a) preparing a medical device by:

(i) coating at least a portion of the medical device with a cationic polyelectrolyte carrier to form a layer of a cationic polyelectrolyte carrier;

(ii) washing the layer of a cationic polyelectrolyte carrier with a washing solution;

(iii) adsorbing at least one negatively charged therapeutic agent effective to induce the growth of blood vessels onto the layer of a cationic polyelectrolyte

carrier to form a layer of at least one negatively charged therapeutic agent; and

~~optionally~~

(iv) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of a cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of the least one negatively charged therapeutic agent has been adsorbed onto the medical device~~.~~; and

(b) implanting the medical device into the target location in a mammal[;]

wherein the at least one negatively charged therapeutic agent is a DNA coding for an angiogenic protein.

67. (Cancelled)

68. (Cancelled)

69. (Cancelled)

70. (Cancelled)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **(703) 305-2024**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Deborah Reynolds*, may be reached at **(703) 305-4051.**

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is **(703) 305-7401**.

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Please note that the examiner is expected to move to a new US PTO office building located in Alexandria on January 12, 2004. The examiner office phone number at the new building is 571-272-0731.

Dave Nguyen
Primary Examiner
Art Unit: 1632

DAVE T. NGUYEN
PRIMARY EXAMINER

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